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Current Approaches to Non-Invasive Ventilation in Critically Ill Patients

Non-invasive ventilation is extensively employed in the management of acute hypoxaemic and hypercapnic respiratory failure, offering a potential means to circumvent intubation in carefully selected patients under vigilant supervision.

Non-Invasive Ventilation

Non-invasive ventilation (NIV) represents a respiratory support strategy designed to alleviate respiratory distress without the need for invasive procedures, utilising a range of interfaces (**Figure 1**). This method involves the provision of continuous positive airway pressure (CPAP), sometimes supplemented with pressure support (PSV) during inspiration, with the primary objective of enhancing both oxygenation and ventilation. Widely adopted for the treatment of acute respiratory failure (ARF), encompassing both hypoxaemic and hypercapnic conditions, particularly in critically ill patients, NIV has demonstrated efficacy in reducing the incidence of intubation and mortality.

NIV is strongly advocated for managing conditions such as cardiogenic pulmonary oedema and exacerbations of chronic obstructive pulmonary disease (COPD) accompanied by hypercapnia. However, its applicability extends to various aetiologies of ARF, including acute respiratory distress syndrome (ARDS), viral or bacterial pneumonia, asthma exacerbations, neuromuscular disorders, thoracic trauma, and mitigating the risk of extubation failure in high-risk patients, among others. Effective NIV implementation hinges on appropriate settings and diligent monitoring to optimise outcomes.

The overarching goals of NIV encompass enhancing minute ventilation (V_{min}), lessening the workload on respiratory muscles to mitigate fatigue, augmenting oxygen diffusion at the alveolar level by elevating the pressure gradient, averting or minimising alveolar collapse, enhancing respiratory system compliance (CRS), optimising oxygenation, and ameliorating hypercapnia.

Indications for Initiating NIV

The decision to initiate NIV should consider the following:

1. **Clinical expertise:** Healthcare professionals should possess training in NIV device utilisation and ventilator management. They must also adeptly interpret patient data to assess objective and subjective progression.
2. **Facility and staffing:** NIV implementation necessitates a well-staffed area capable of continuous monitoring and prompt intervention in case of failure, requiring advanced airway management. Adequate equipment for rapid intubation sequences and invasive mechanical ventilation should be readily accessible.
3. **Equipment availability:** While various interface types and sizes exist, no single device demonstrates clear superiority. It is paramount to select an interface suited to individual patient needs, ensuring good tolerance and minimal leak-age or damage.
4. **Evidence-based practice:** The choice to employ NIV should align with the best available evidence for each specific pathology. For conditions like COPD exacerbation or acute cardiogenic pulmonary oedema, NIV yields higher success rates compared to pathologies with slower resolution, such as severe viral pneumonia (e.g., severe COVID-19).

Table 1 summarises indications for NIV utilisation, while **Table 2** outlines contraindications.

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Hypercapnic Respiratory Failure

Acute exacerbation of Chronic Obstructive Pulmonary Disease (*Evidence Level 1A*)

Asthma crisis (*Evidence Level D*)

Acute decompensation of obesity hypoventilation syndrome (*Evidence Level 3B*)

Hypoxaemic Acute Respiratory Failure

Cardiogenic acute pulmonary oedema (*Evidence Level 1A*)

Acute Respiratory Distress Syndrome (ARDS) (*Evidence Level 2B*)

Viral or bacterial pneumonia (*Evidence Level 2B*)

Acute respiratory failure in immunocompromised patients (*Evidence Level 2B*)

Special Scenarios

Prevention of respiratory failure post-extubation in high-risk patients (*Evidence Level 2B*)

Perioperative in at-risk patients (*obesity, COPD*) (*Evidence Level 2A*)

Dyspnoea relief in palliative care (*Evidence Level 2A*)

Pre-oxygenation prior to intubation in at-risk patients (*obesity, COPD*) (*Evidence Level 2B*)

Pre-oxygenation prior to emergency intubation (*Evidence Level 1B*)

Table 1. Indications for non-invasive mechanical ventilation use. Modified from Chawla et al. 2020.

Chronic Obstructive Pulmonary Disease

The use of NIV is recommended for managing acute exacerbations of COPD in patients meeting at least one of the following criteria (GOLD 2024 guidelines):

- Respiratory acidosis ($\text{PaCO}_2 \geq 6.0$ kPa or 45 mmHg and arterial $\text{pH} \leq 7.35$)
- Severe dyspnoea accompanied by clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as the use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces
- Persistent hypoxaemia despite supplemental oxygen therapy

The GOLD Guidelines 2024 advocate for NIV as the primary ventilation mode for addressing acute respiratory failure in hospitalised patients with acute COPD exacerbations. This recommendation is supported by randomised controlled trials demonstrating a success rate ranging from 80% to 85%.

Utilisation of NIV in COPD exacerbations yields several beneficial outcomes, including enhanced oxygenation, reduction of acute respiratory acidosis, decreased respiratory rate, alleviation of respiratory work and breathlessness. Furthermore, it contributes to a diminished incidence of ventilator-associated pneumonia (OR 0.26, 95% CI 0.08–0.81) and shorter hospital stays. Importantly, NIV significantly reduces mortality rates (RR 0.63, 95% CI 0.46–0.87) and the necessity for endotracheal intubation (RR 0.41, 95% CI 0.33–0.52).

Cardiogenic Acute Pulmonary Oedema

In patients experiencing cardiogenic acute pulmonary oedema, the utilisation of non-invasive ventilation (NIV) has demonstrated significant benefits, including a reduction in mortality (RR 0.80, 95% CI: 0.66–0.96) and a decrease in the requirement for intubation (RR 0.60, 95% CI: 0.44–0.80) (Rochweg et al. 2017). This conclusion is supported by a systematic review conducted by Masip et al. in 2015, which analysed 15 randomised controlled trials encompassing 727 patients across 10 different countries. The review revealed a noteworthy decrease in in-hospital mortality

and the necessity for intubation when employing NIV in cases of cardiogenic acute pulmonary oedema.

NIV as Preoxygenation in Emergency Intubation

When a patient has failed NIV and the decision is made to proceed with intubation, NIV can serve as a preoxygenation strategy. The PREOXY study (Gibbs et al. 2024) demonstrated that preoxygenation with non-invasive ventilation resulted in a lower incidence of hypoxaemia during intubation compared to preoxygenation with an oxygen mask (difference, -9.4 percentage points; 95% CI: -13.2 to -5.6; $P < 0.001$). Additionally, there was a reduction in mortality with no significant difference in adverse events. The strategy employed involved setting 5 cmH_2O of CPAP, 10 cmH_2O of inspiratory pressure, and $\text{FiO}_2:1$ for 3 minutes prior to pharmacological induction.

Post-Surgical Patients

Anaesthesia and postoperative pain following major surgical procedures can precipitate postoperative pulmonary complica-

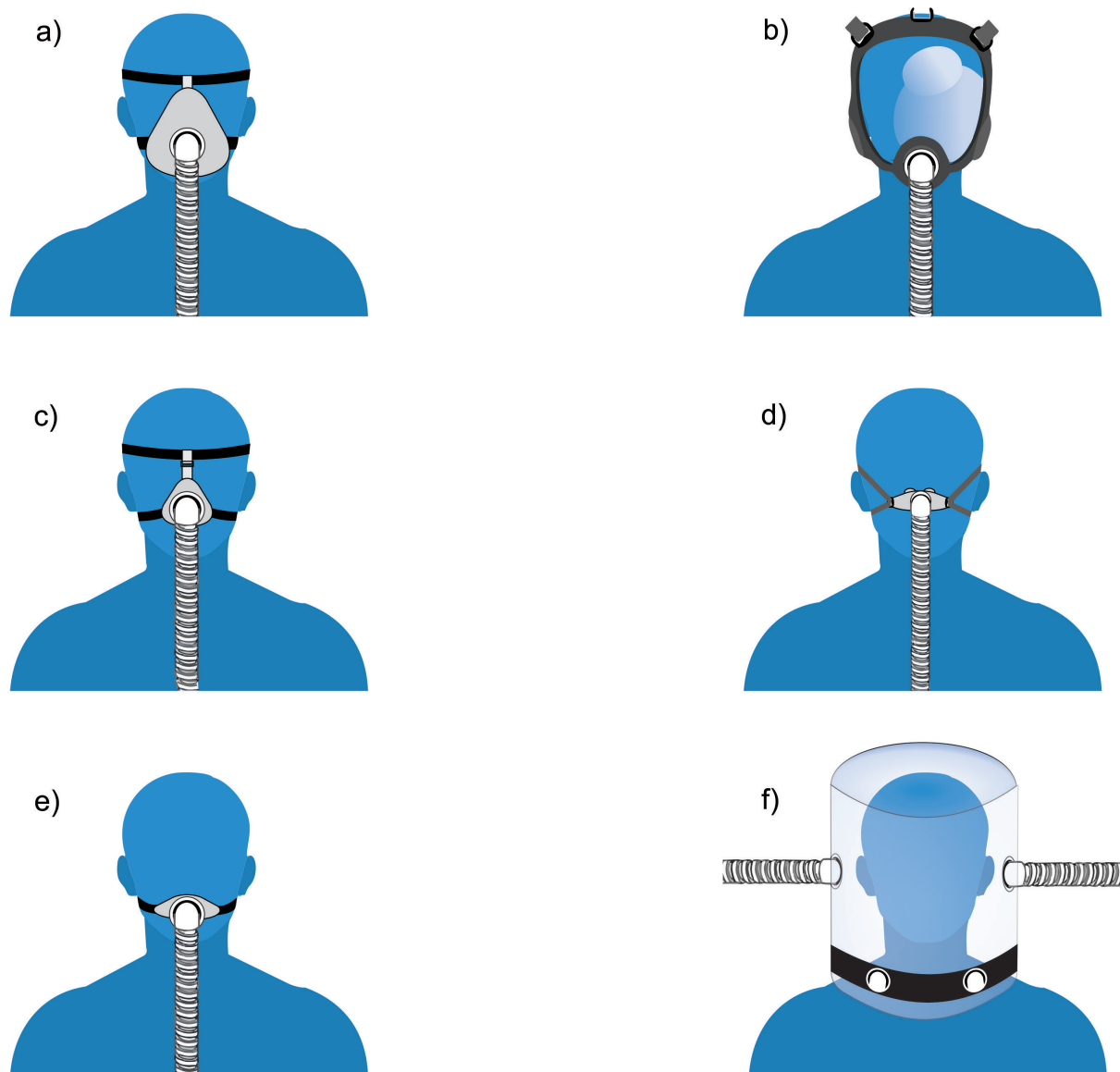


Figure 1. The NIV interfaces are a) oronasal mask, b) total-face mask, c) nasal mask, d) nasal pillows, e) mouthpiece, and f) helmet

tions, including atelectasis, hypoxaemia, hypercapnia, reduced lung volume, and diaphragm dysfunction. These alterations typically manifest during the early postoperative period, with diaphragm dysfunction potentially persisting for up to 7 days. Maintaining adequate oxygenation and alleviating dyspnoea in the postoperative period are crucial objectives. Imaging studies have demonstrated that the utilisation of NIV can enhance pulmonary aeration and mitigate atelectasis in patients undergoing major abdominal surgery postoperatively.

In a randomised clinical trial (Auriant et al. 2001) it was found that among patients experiencing respiratory failure during the postoperative period following lung resection surgeries for cancer, NIV significantly reduced the necessity for re-intubation and decreased hospital mortality rates.

Moreover, early implementation of CPAP has been shown to markedly decrease the incidence of re-intubation, reducing it from 10% to 1% ($p=0.005$) in patients experiencing acute respiratory failure after abdominal surgery (Rochwerg et al. 2017).

Relief of Dyspnoea in Palliative Care

In palliative care settings, certain terminally ill patients, such as those with metastatic lung cancer, may experience chronic dyspnoea, with the intensity often increasing as death approaches. While opioids and benzodiazepines are commonly employed to alleviate this symptom, they may lead to undesirable effects like excessive sedation. NIV is deemed effective if it can ameliorate dyspnoea without causing discomfort from the interface or prolonging life unnecessarily (Rochwerg et al. 2017). Studies have indicated that NIV can improve dyspnoea, as measured by the Borg scale (mean difference 0.89 lower, 95% CI 0.79-0.99 lower; moderate certainty), and results in decreased morphine requirements (mean difference 32.4 mg lower, 95% CI 17.4-47.4 lower; low certainty) (Rochwerg et al. 2017).

Immunocompromised Patients With Acute Respiratory Failure

Meta-analyses by Huang et al. (2017) and Wang et al. (2016) demonstrate that early initiation of NIV is effective in reducing hospital and 30-day mortality rates in selected immunocom-

promised patients with acute respiratory failure. Additionally, a systematic review (Zayed et al. 2019) shows that NIV is associated with a significant decrease in intubation rates in this patient population.

COVID-19 Pneumonia

In the RECOVERY study, it was found that the need for endotracheal intubation or mortality at 30 days was significantly lower in the NIV-treated group (36.3%; 137 of 377 participants) compared to those receiving conventional oxygen therapy (44.4%; 158 of 356 participants) (absolute difference, -8% [95% CI, -15% to -1%], $P = .03$). Researchers utilised 8 cm H₂O of continuous positive airway pressure (CPAP) delivered via ventilators or outpatient CPAP devices (Perkins et al. 2022).

Thoracic Trauma

A study randomly assigning patients with thoracic trauma and acute respiratory failure to NIV treatment demonstrated a significantly lower intubation rate in the NIV group (RR 0.20, 95% CI: 0.05-0.87), leading to a substantial reduction in ICU length of stay (Hernandez et al. 2010).

Prevention of Extubation Failure

The utilisation of NIV can be contemplated as a preventive measure against respiratory failure following extubation, particularly in high-risk patients such as those with COPD, heart disease, obesity, ARDS, among others. The advantages of early NIV application post-extubation have been assessed in patients exhibiting certain risk factors (Rochwerf et al. 2017):

- Patients aged over 65 years or those with underlying cardiac or respiratory conditions.
- Non-invasive ventilation is recommended to aid weaning from mechanical ventilation in patients with hypercapnic respiratory failure (conditional recommendation, moderate certainty of evidence).
- It may be employed in obese and hypercapnic individuals with obesity hypoventilation syndrome and/or right heart failure in the absence of acidosis.

Neurological

Altered state of alertness (stupor, coma)
Loss of protective airway reflexes
Agitation or delirium
Post-seizure state, stroke
Acute polyradiculoneuropathies (e.g., rapidly progressive Guillain-Barré syndrome affecting respiratory muscles or cranial nerves)

Respiratory

Life-threatening hypoxaemia
Inability to handle secretions
Intolerance to NIV

Haemodynamic

Circulatory shock
Uncontrolled arrhythmias

Gastrointestinal

Intestinal obstruction
Haematemesis
Persistent vomiting

Facial

Lacerations
Fractures of facial bones with instability
Burns

Table 2. Contraindications for the use of non-invasive mechanical ventilation

Setting up NIV

COPD Exacerbation

Start with pressure support ventilation (PSV) settings of 5-8 mm H₂O and continuous positive airway pressure (CPAP) of 5 cm H₂O, adjusting as needed to achieve a respiratory rate < 20 per minute and a tidal volume of 6 to 8 ml/kg of predicted body weight.

- Monitor pH and consciousness state (Rittayamai et al. 2022) closely during the first and second hours. Adjust trigger sensitivity to minimise patient-ventilator asynchrony, particularly avoiding ineffective efforts to activate the trigger.

Cardiogenic Acute Pulmonary Oedema

- Apply an initial CPAP of 5 to 10 cm H₂O, with a maximum increase of up to 15 cm H₂O, based on the patient's tidal volume requirements.
- Provide an initial inspired oxygen fraction (FiO₂) of 0.50, which can be adjusted upwards if peripheral arterial oxygen saturation (SpO₂) remains below 94% (Gray 2008).

ARDS

- Initiate with CPAP set at 10 cm H₂O and FiO₂ of 0.6. Avoid pressure support ventilation to mitigate the risk of volutrauma,

maintaining a low tidal volume (<6 to 8 ml/kg of predicted body weight) to minimise lung injury.

- Subsequently, adjust FiO₂ to attain a SpO₂ target of 88 to 92%.

COVID-19

Programme a CPAP level of 8 cm H₂O without PSV and with the minimum FiO₂ required to maintain a target SpO₂ of 92% to 96% (RECOVERY-RS 2022).

It's important to note that none of these NIV configuration suggestions are standardised universally or supported by large controlled randomised trials, emphasising the crucial role of clinical judgement and expertise in managing these patients (Table 3).

Monitoring During NIV

In accordance with the LUNG SAFE study, patients with ARDS who encounter NIV failure and delays in intubation face a mortality rate of up to 45%, underscoring the necessity for validated tools to promptly assess the risk of failure in these patients (Bellani et al. 2017).

Upon initiation of NIV, continuous monitoring akin to that of any intensive care unit patient is imperative, even outside of such a unit. This monitoring encompasses various clinical and biochemical parameters alongside observation of each patient's signs and symptoms.

It is advisable to regularly evaluate whether the patient remains a suitable candidate for maintaining this ventilatory support. Parameters such as patient comfort, tolerance to the ventilation interface, respiratory rate, and oxygen saturation should be assessed every 30 minutes during the initial 6 to 12 hours after commencing non-invasive mechanical ventilation, and thereafter every hour. Additionally, the patient's level of consciousness can be gauged using tools such as the Glasgow Coma Scale or the Kelly-Matthay Score (Piraino 2021).

Delirium, linked with NIV failure, ought to be assessed daily and routinely employing validated scales like the CAM-ICU.

Condition	Parameters and Settings	Desired Effect	When to Decide on Intubation
Acute Decompensated Heart Failure	CPAP: 5 -15 cm H ₂ O adjusted according to the patient's tidal volume needs. FiO ₂ : 0.50 can be increased if SpO ₂ remains below 94%.	Improve myocardial performance and respiratory mechanics	At 1–2h: Depressed mental status, Respiratory fatigue despite optimal NIRS. HACOR Score >5
Acute Exacerbation of COPD	PS: up to 10-18 cmH ₂ O CPAP: 5 cmH ₂ O Target: Tidal Volume 10-15 ml/kg of predicted body weight and RR <20 per minute	Offset autoPEEP, reduce work of breathing, improve ventilation	At 1–2h: Respiratory fatigue despite optimal NIRS, Depressed mental status, Severe respiratory acidosis (pH < 7.2) HACOR Score >5
Acute Hypoxaemic Respiratory Failure	Begin: CPAP:10 cm H ₂ O Adjusted to low tidal volume (<6 to 8 ml/kg of predicted body weight) to reduce damage. FiO ₂ : 0.6 Should be adjusted to achieve a SpO ₂ target of 88 to 92.	Improve FRC, V/Q mismatch, reduce respiratory effort	HACOR Score >5 High respiratory effort, Tachypnoea (RR > 30) despite maximal support, Hypoxaemia (SpO ₂ < 90%)

Table 3. NIV Configuration recommendations for various respiratory conditions. Modified from Mosier et al. 2024.

Abbreviations: CPAP = Continuous Positive Airway Pressure, FiO₂ = Fraction of Inspired Oxygen, FRC = Functional Residual Capacity, V/Q = Ventilation/Perfusion, NIRS = Non-Invasive Respiratory Support, RR = Respiratory Rate.

Arterial blood gas analysis, regarded as the gold standard for monitoring respiratory failure, is advised one hour post-initiation of non-invasive ventilation. Alterations in pH and the paO₂/FiO₂ ratio serve as pivotal prognostic indicators in cases of acute respiratory failure.

Duan et al. (2017) identified the most pertinent parameters for predicting NIV success in patients with hypoxaemic ARF and proposed a scoring system termed HACOR. The HACOR score integrates clinical and biochemical parameters such as heart rate, pH, level of consciousness, paO₂/FiO₂ ratio, and

Variable	Value	Score
Heart rate (HR)	≤120	0
	>120	1
Acidosis (pH)	>7.35	0
	7.30-7.34	2
	7.25-7.29	3
	<7.25	4
Consciousness (GCS)	15	0
	13-14	2
	11-12	5
	<10	10
Oxygenation (PaO ₂ /FiO ₂)	>200	0
	176-200	2
	151-175	3
	126-150	4
	101-125	5
	101-125	5
Respiratory rate (RR)	≤30	0
	31-35	1
	36-40	2
	41-45	3
	>45	4

Table 4. HACOR scale for the success of non-invasive mechanical ventilation in patients with COPD.

respiratory rate. A HACOR score exceeding 5 calculated within the first hour of NIV predicts treatment failure, exhibiting an area under the curve of 0.91, specificity of 92.6%, and sensitivity of 75.9% (Table 4).

As part of monitoring, vigilance toward adverse effects is paramount. Notably, those requiring scrutiny include interface disconnection, gastric distension, secretion expulsion, pneumonia, and pneumothorax.

It is imperative to recognise that monitoring alone does not suffice to alter patient outcomes; rather, it is the actions informed by this information that make the difference in patient care.

Considerations for the Use of NIV

Several authors have pointed out that certain facial features, such as the presence of a beard or the placement of orotracheal and nasotracheal tubes, may impede achieving an airtight seal between the interface and the patient's face, potentially being considered a contraindication for non-invasive ventilation use. However, this condition is often viewed as a relative contraindication. The priority should be to ensure an airtight seal by utilising an interface appropriate to the patient's size and, if necessary and feasible, considering the removal of facial hair.

A primary consequence of a poor airtight seal is the occurrence of leaks, which can affect both the delivered volume and the cycling of the ventilator. Initially, adjusting the headband can address this issue, but it's important to note that relying solely on this measure can cause discomfort and intolerance to the interface and may even lead to the formation of ulcers on the nasal bridge. Some ventilators have systems designed to compensate for these leaks.

It's relevant to mention that NIV programming with support mode typically exhibits better compensation capability compared to volume-based programming. When using flow-cycled ventilation, leaks can hinder achieving the programmed expiratory trigger, resulting in a prolongation of inspiratory time. Time-cycled settings can reduce the patient's respiratory effort and have been associated with better interaction between the patient and the ventilator (Calderini et al. 1999).

Success and Failure of NIV

NIV represents a useful and cost-effective method for reducing

the need for intubation in patients with acute respiratory failure (ARF), heart failure, and exacerbation of COPD. However, it is well documented in the literature that its use without the application of success or failure predictors is associated with delays in intubation and, therefore, increased mortality. For this reason, there has been a constant effort in developing tools to predict the outcome of NIV.

In the case of COPD, failure rates ranging between 15% and 24% have been reported in previous studies. These studies have identified multiple variables that can predict NIV failure in COPD patients, such as disease severity, heart rate, respiratory rate, consciousness state, and blood pH. These independent factors have been integrated into what is known as the HACOR score.

Additionally, a multicentre study has demonstrated that various parameters are associated with a high risk of NIV failure, including high severity scores (e.g., APACHE II and SAPS II), advanced age, lack of improvement one hour post-NIV initiation, multiorgan failure, previous incapacity for self-care, pH of 7.25 or carbon dioxide concentration exceeding 75 mm Hg after 2 hours of NIV commencement, and respiratory failure without an apparent cause.

Regarding the success of NIV, positive predictors such as improvement in pH in the first hour of therapy, a decrease in respiratory rate, and a reduction in carbon dioxide levels are associated with a positive response to NIV.

Discontinuation of NIV

Similar to invasive mechanical ventilation, specific criteria for early NIV withdrawal are crucial to mitigate associated complications. After resolving the cause of ARF, the following withdrawal criteria should be sought: adequate oxygenation (PaO₂/FiO₂ > 200 mmHg during NIV with FiO₂ 0.5), pH > 7.35, respiratory rate < 25 without the use of accessory respiratory muscles, haemodynamic stability (assessed via heart rate and blood pressure), Kelly score ≤ 2, and absence of respiratory distress signs such as agitation, diaphoresis, or anxiety.

Additionally, another crucial criterion for NIV withdrawal is

the presence of failure predictors, which may include high disease severity scores (e.g., APACHE II, SAPS II, SOFA), advanced age, lack of improvement post-1 hour with NIV, multiorgan involvement, premorbid state indicating self-care inability, mean pH < 7.25, mean PaCO₂ ≥ 75 mm Hg after 2 hours of NIV initiation in hypercapnic ARF patients, difficulty identifying ARF aetiology (e.g., ARDS, pneumonia), and PaO₂/FiO₂ ratio < 150 mm Hg.

Conclusion

NIV is a supportive strategy for acute respiratory failure that has been shown to reduce intubation rates and mortality in specific populations. Proper programming and constant monitoring are essential.

Conflict of Interest

None.

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